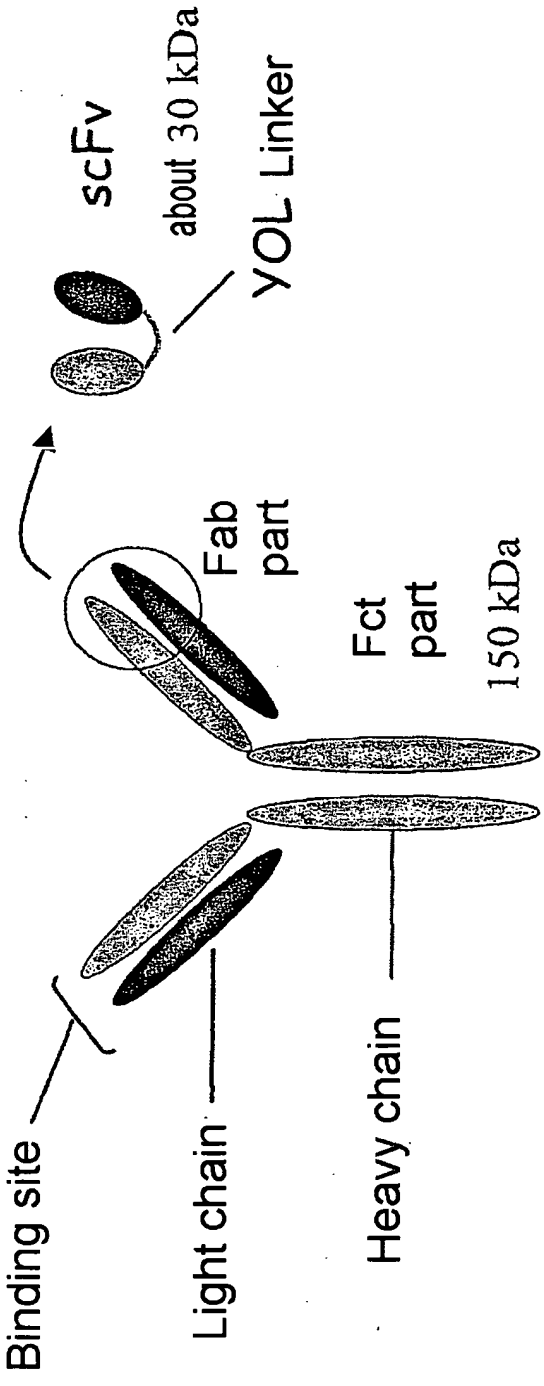

Fig. 1. Schematic representation of an scFv in comparison with the full-length antibody.

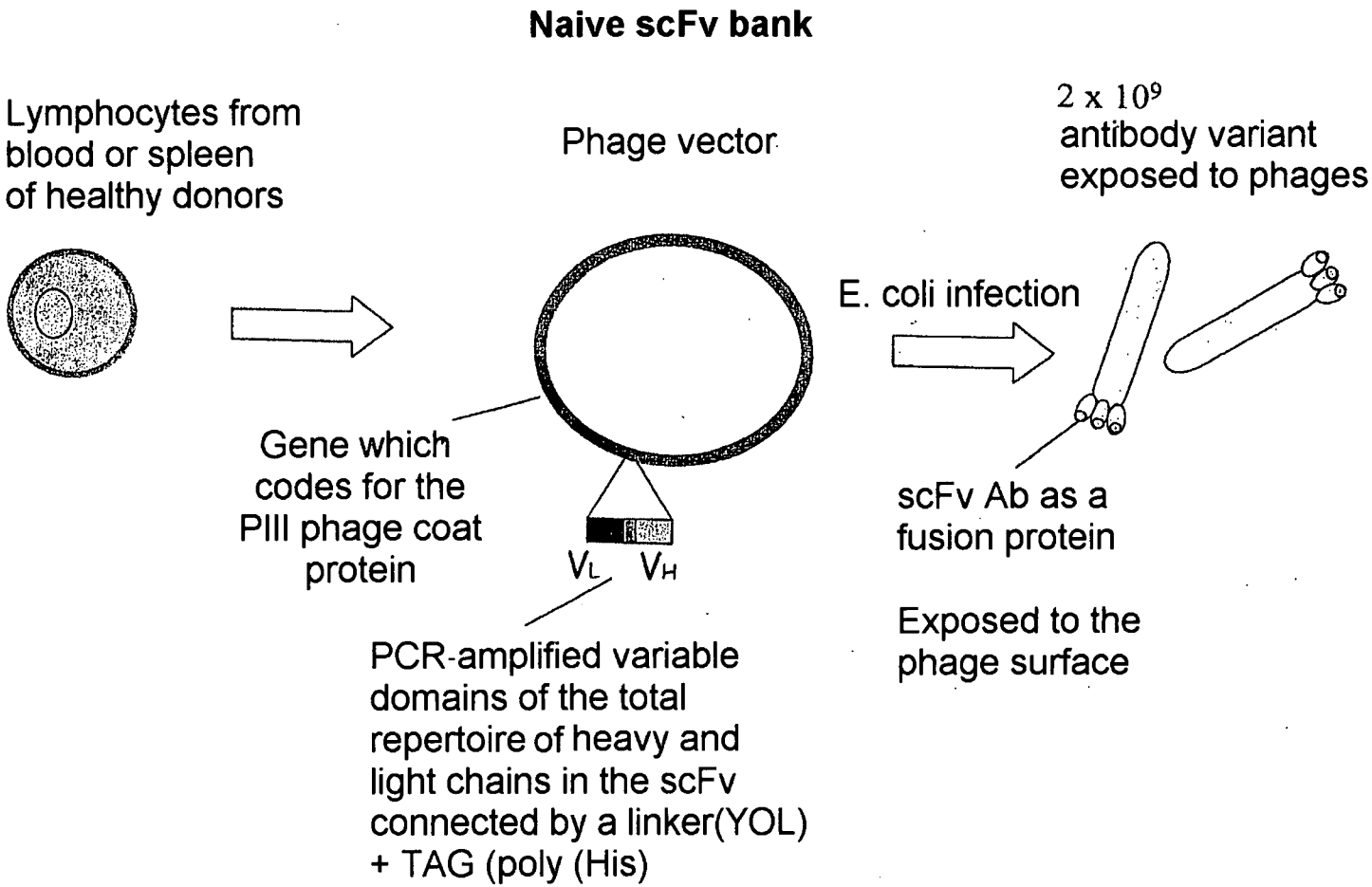

Fig. 2. Schematic representation of the generation of the naive scFv bank from lymphocytes from blood or spleen.

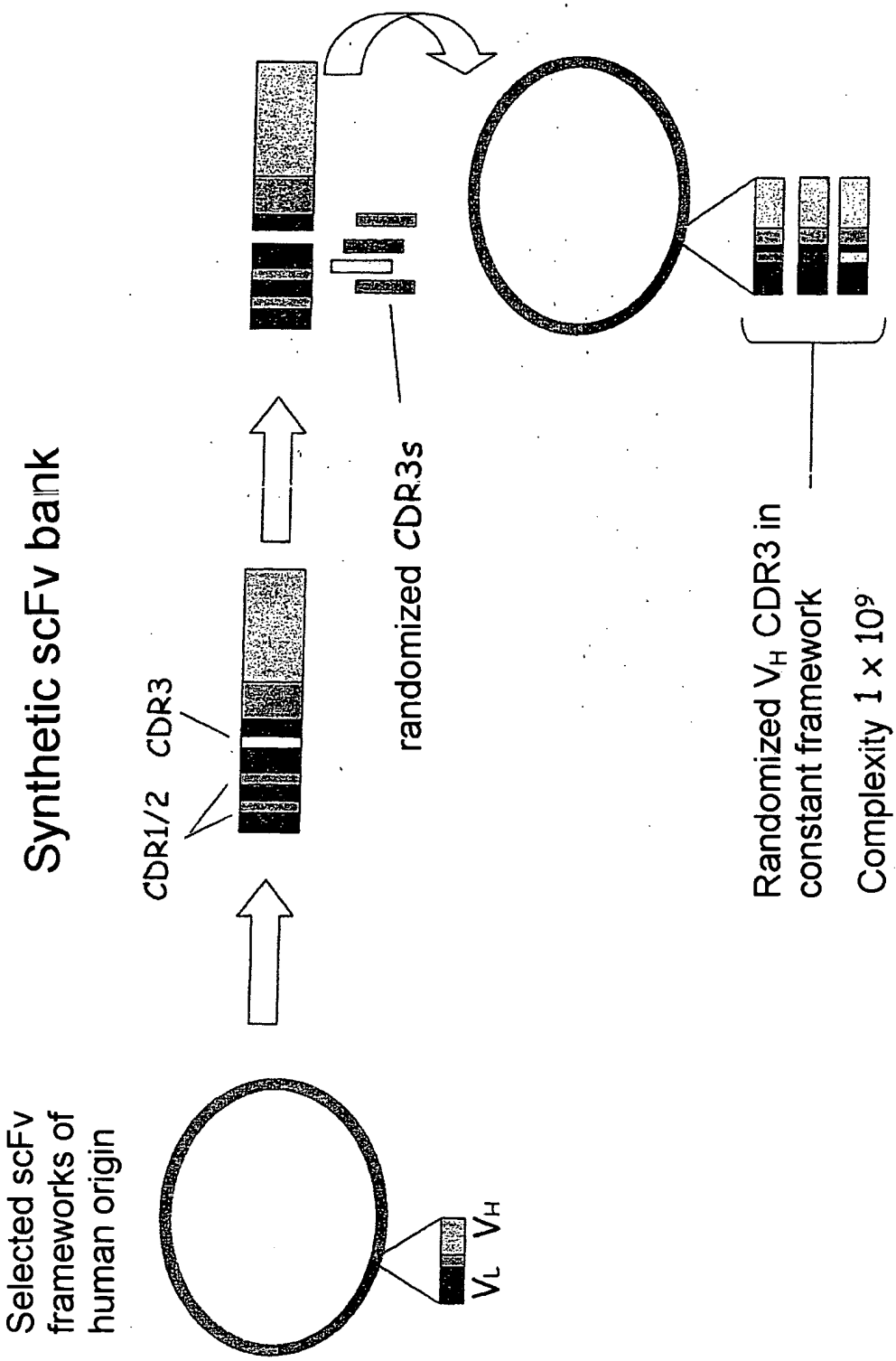

Fig. 3. Schematic representation of the synthetic scFv bank.

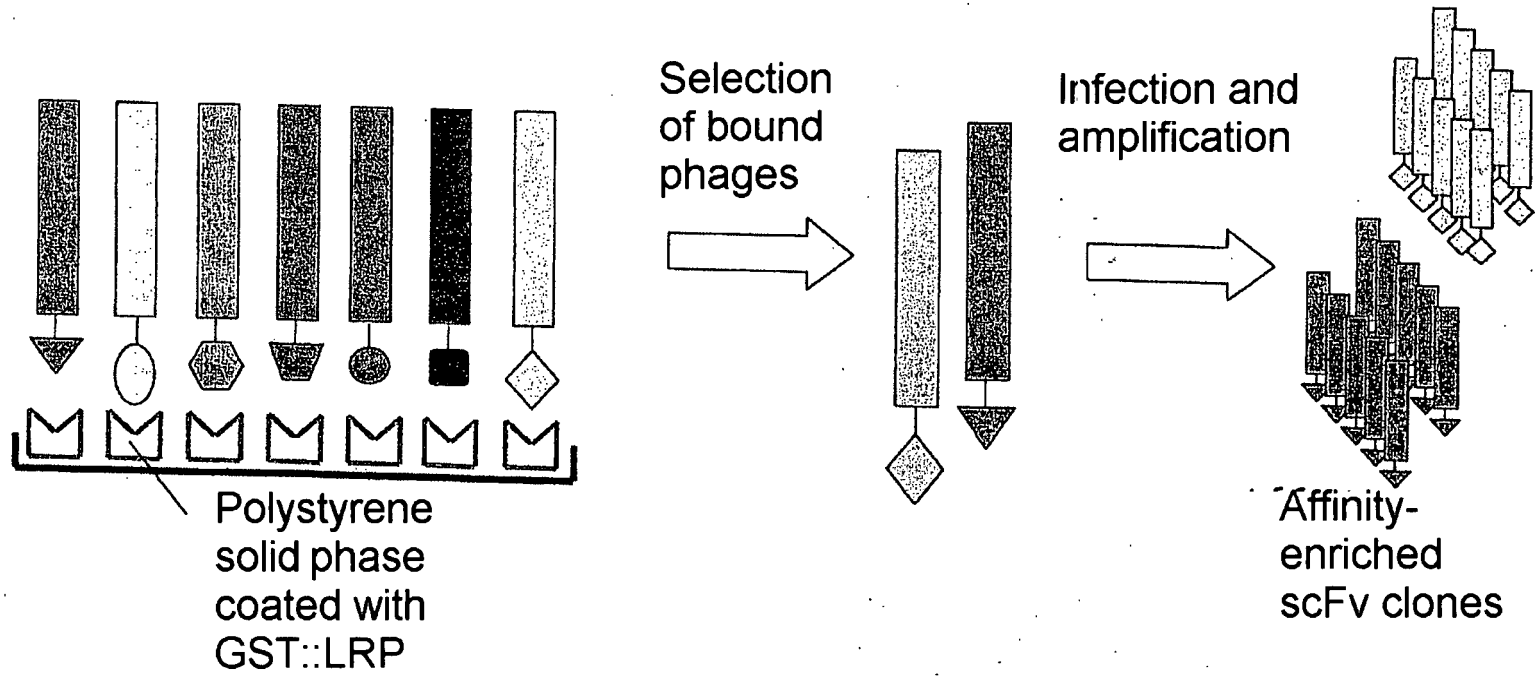

Fig. 4: Schematic representation of the screening of anti-LRP scFv antibodies against GST::LRP by "phage display" using the naive or synthetic scFv banks which are shown in Fig. 1 and Fig. 2.

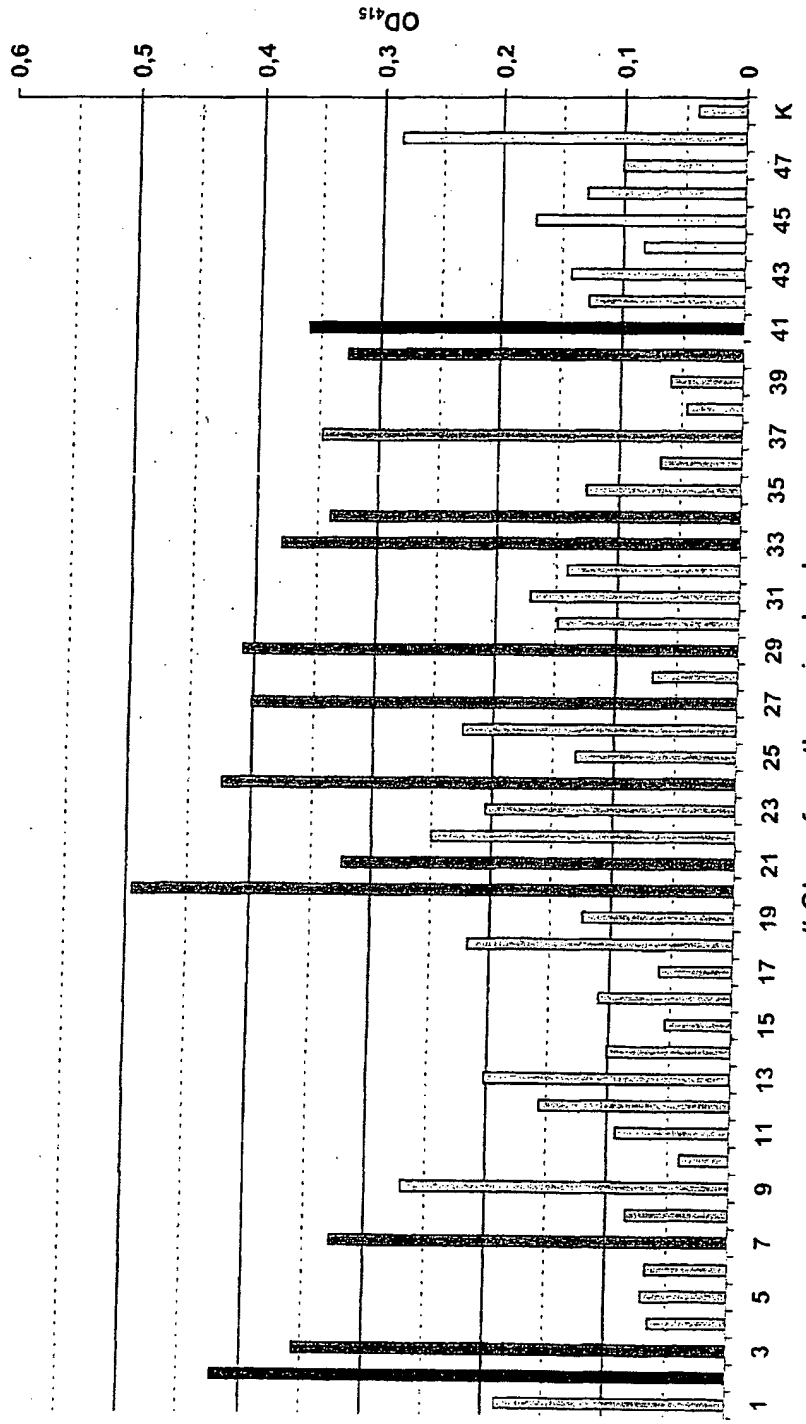

Fig. 5. ELISA of periplasmatic crude extracts of individual clones obtained after three selection rounds from the naive scFv bank

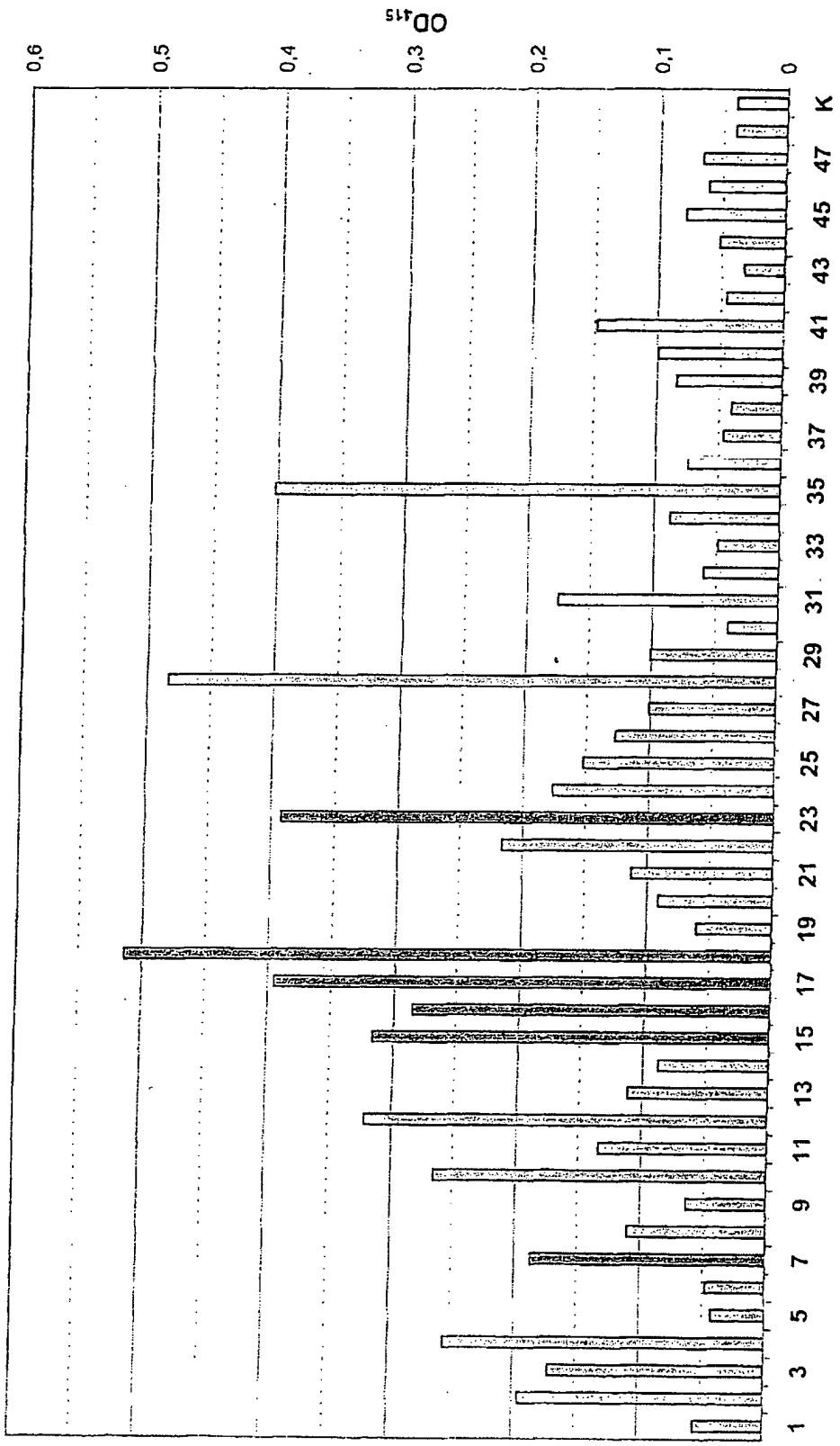

Fig. 6 ELISA of periplasmatic crude extracts of individual clones obtained from the synthetic scFv bank

- Three panning rounds on soluble GST::LRP bound directly to the solid phase
- Identification of individually positive clones in the ELISA

• for GST::LRP fusion, with αHis-HRP
• Fresh testing positively identified clones for GST to the exclusion of GST Specificity

		GST::LRP	GST
ELISA Positive	N	66%	-
	S	53%	-
Selected clones	N	13	neg.
	S	6	neg.
BstN I groups	N	10/13 2/13 1/13	-

Fig. 7. Results of the ELISA from Figs. 5 and 6 after three selection rounds on GST::LRP fusion protein

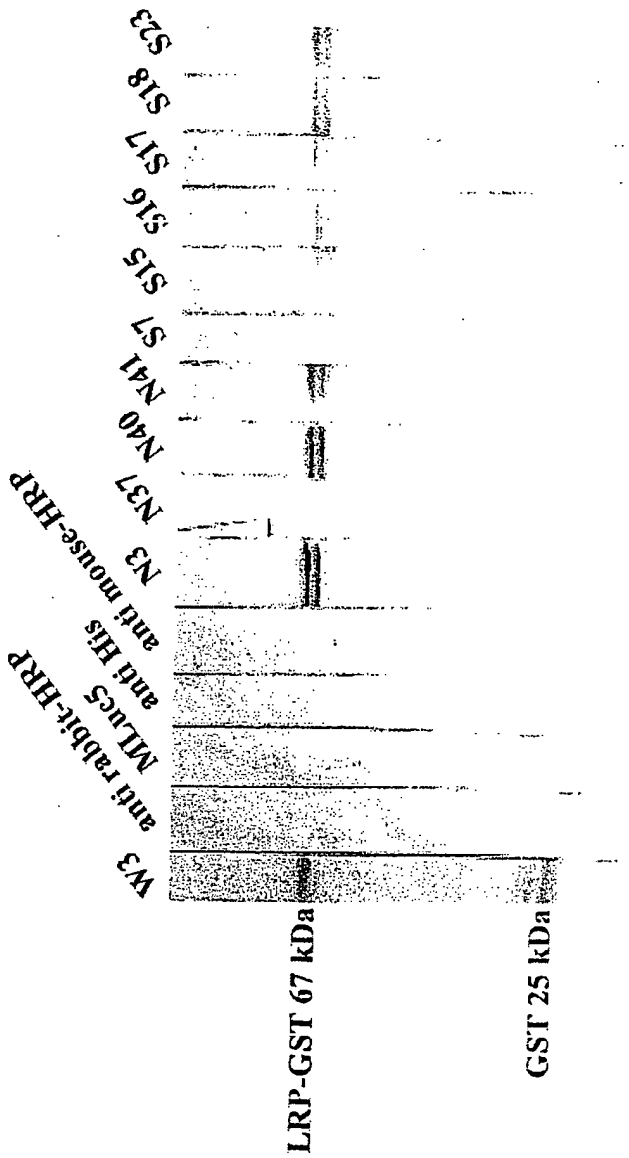

Fig. 8. Western Blot analysis of recombinant GST::LRP/GST detected using scFvs from the naive and synthetic scFv banks

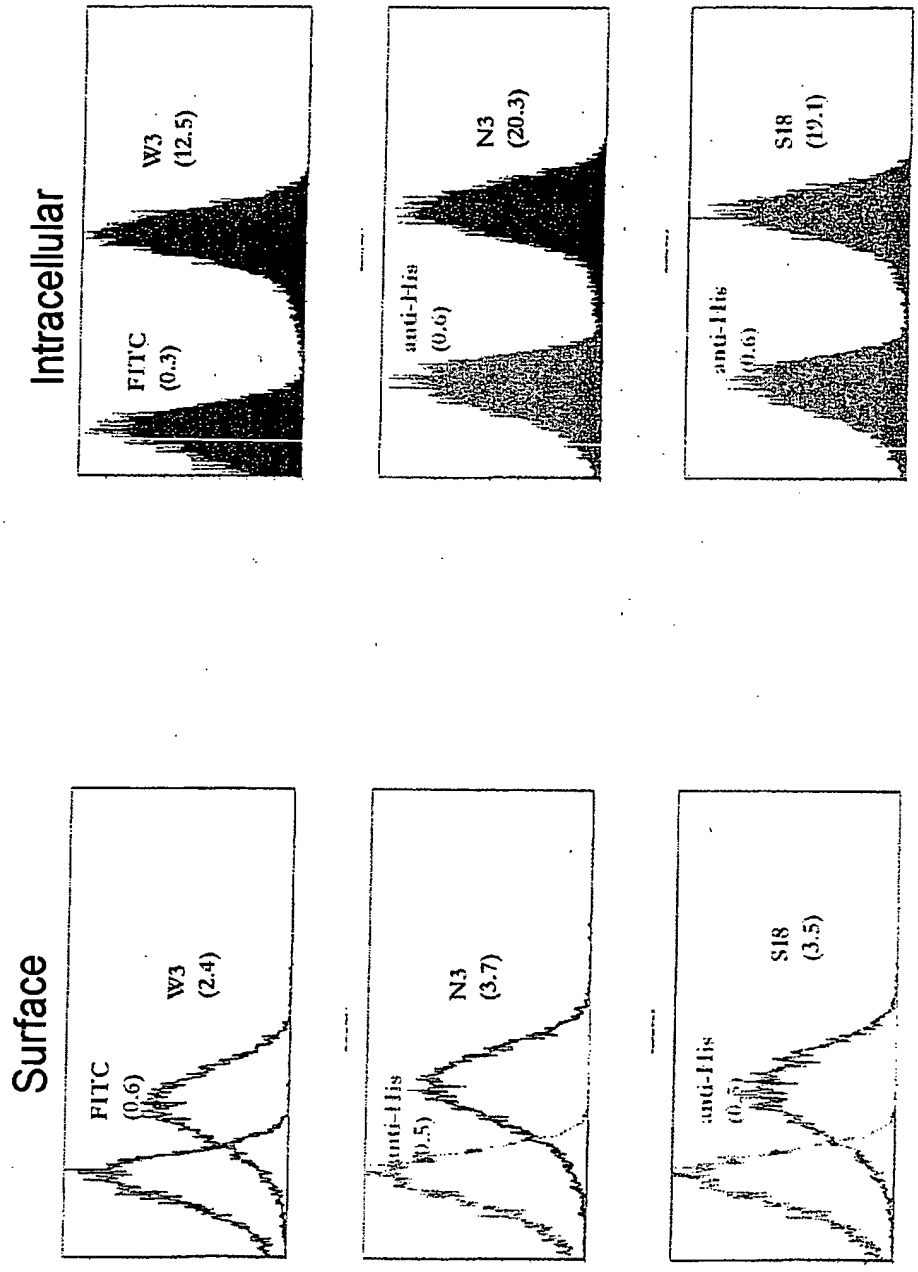

Fig. 9. The antibodies W3, S18 and N3 recognize LRP/LR in and on N2a cells

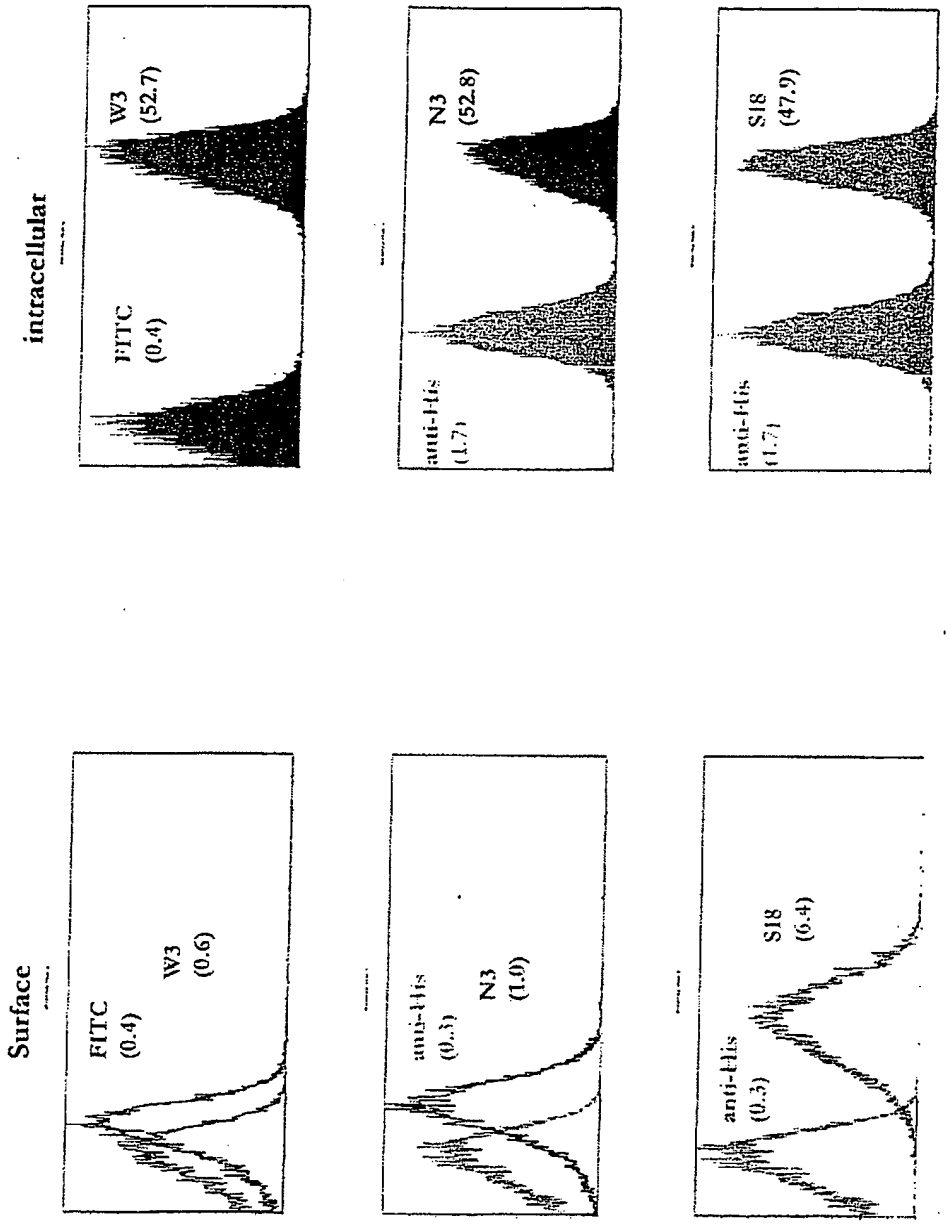

Fig. 10. The antibodies W3, S18 and N3 recognize LRP/LR in and on Jurkat cells

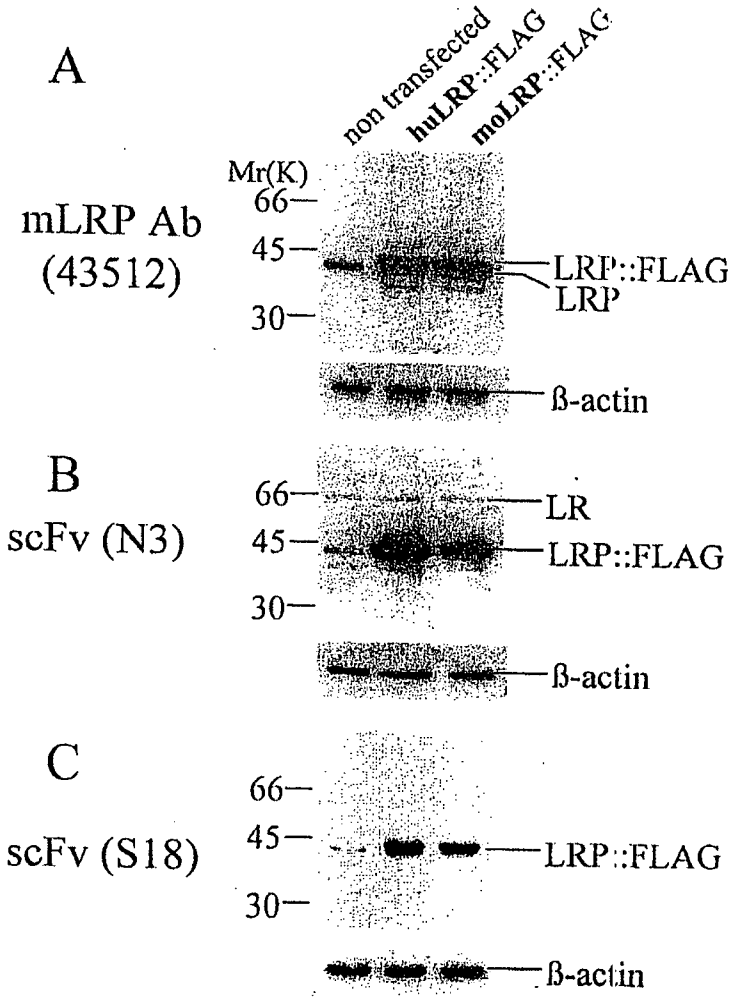

Fig. 11. Western Blot analysis of rec. LRP::FLAG and endogenous LRP/LR in BHK cells transfected with rec. Semliki forest virus RNA

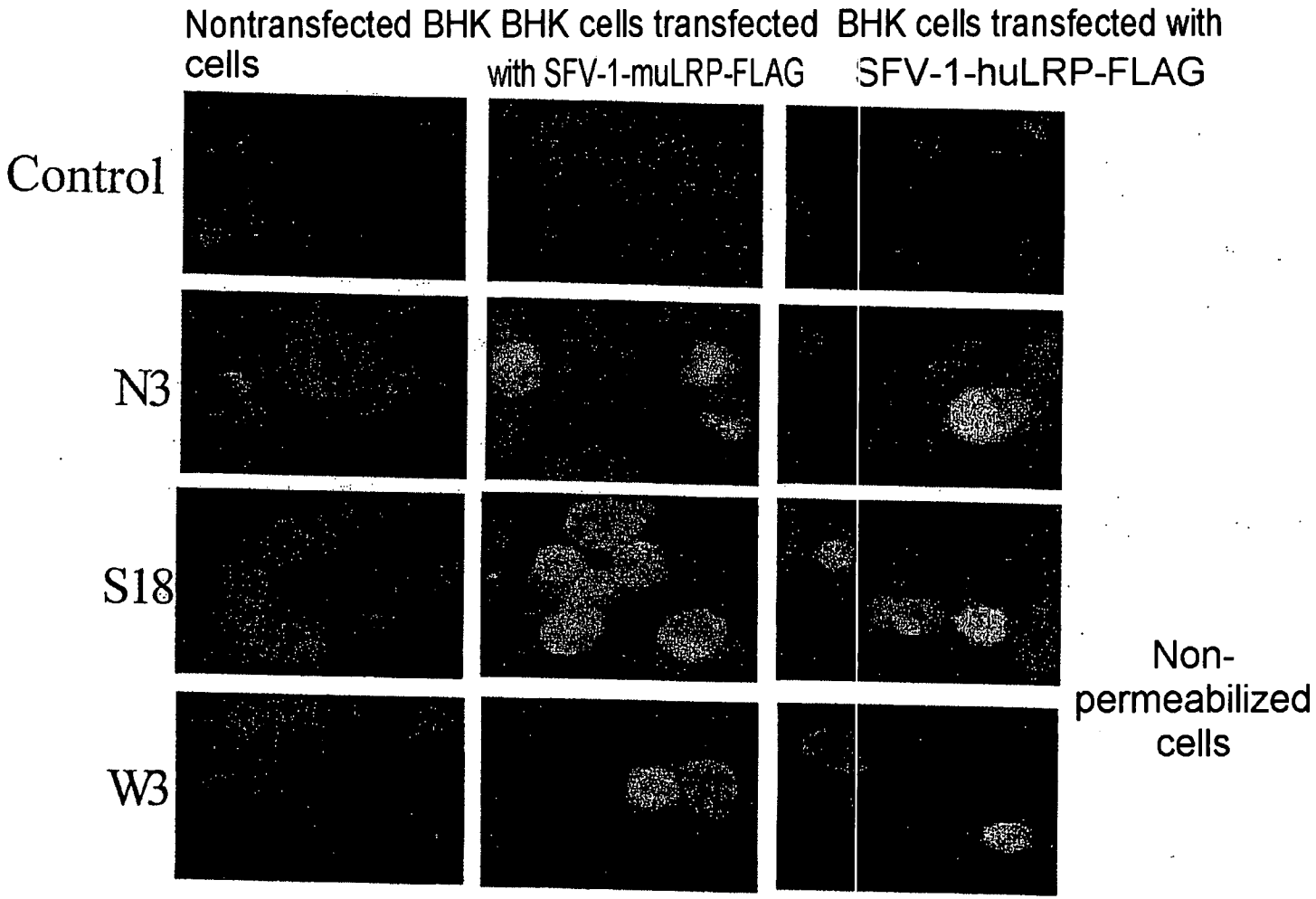

Fig. 12. IF analysis of rec. LRP::FLAG and endogenous LRP/LR on the surface of BHK cells transfected with rec. Semliki forest virus RNAs

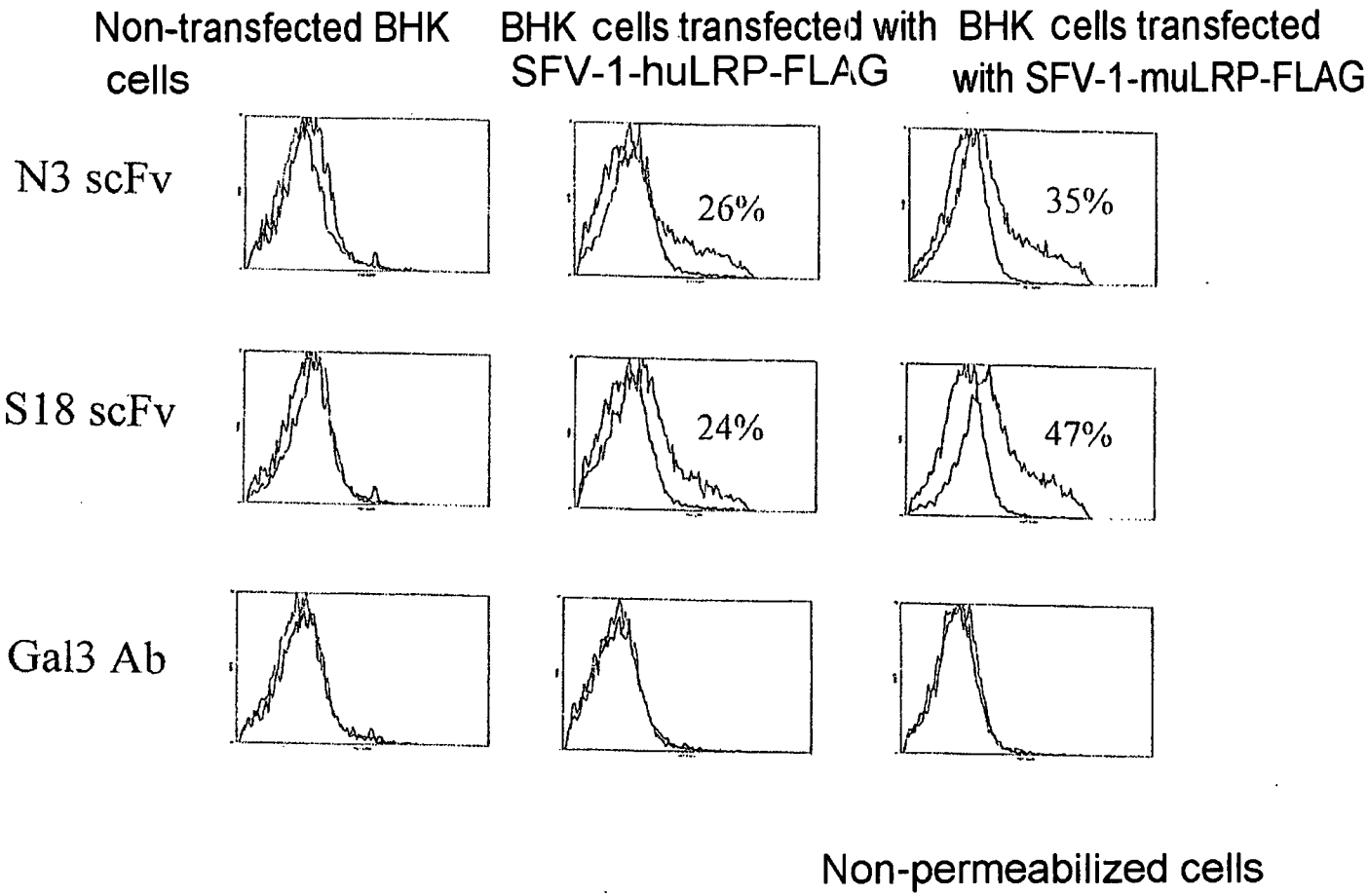

Fig. 13. FACS analysis of rec. LRP::FLAG and endogenous LRP/LR on the surface of BHK cells transfected with rec. Semliki forest virus RNAs

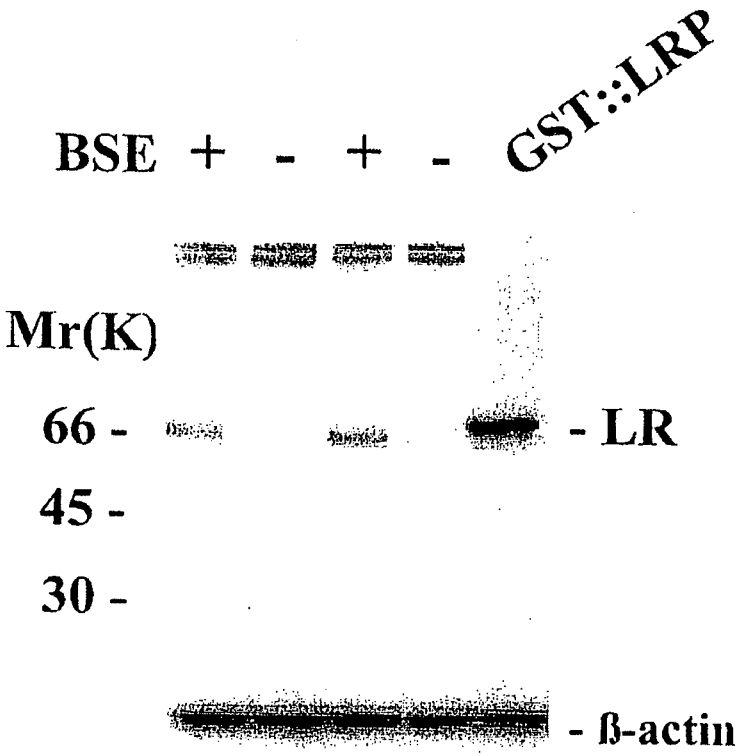

Fig. 14. Recognition of the 67 kDa LR form of the laminin receptor by antibody S18 in the leucocyte fraction of the blood of cattle which are suffering from BSE. + cattle suffering from BSE; - healthy cattle.

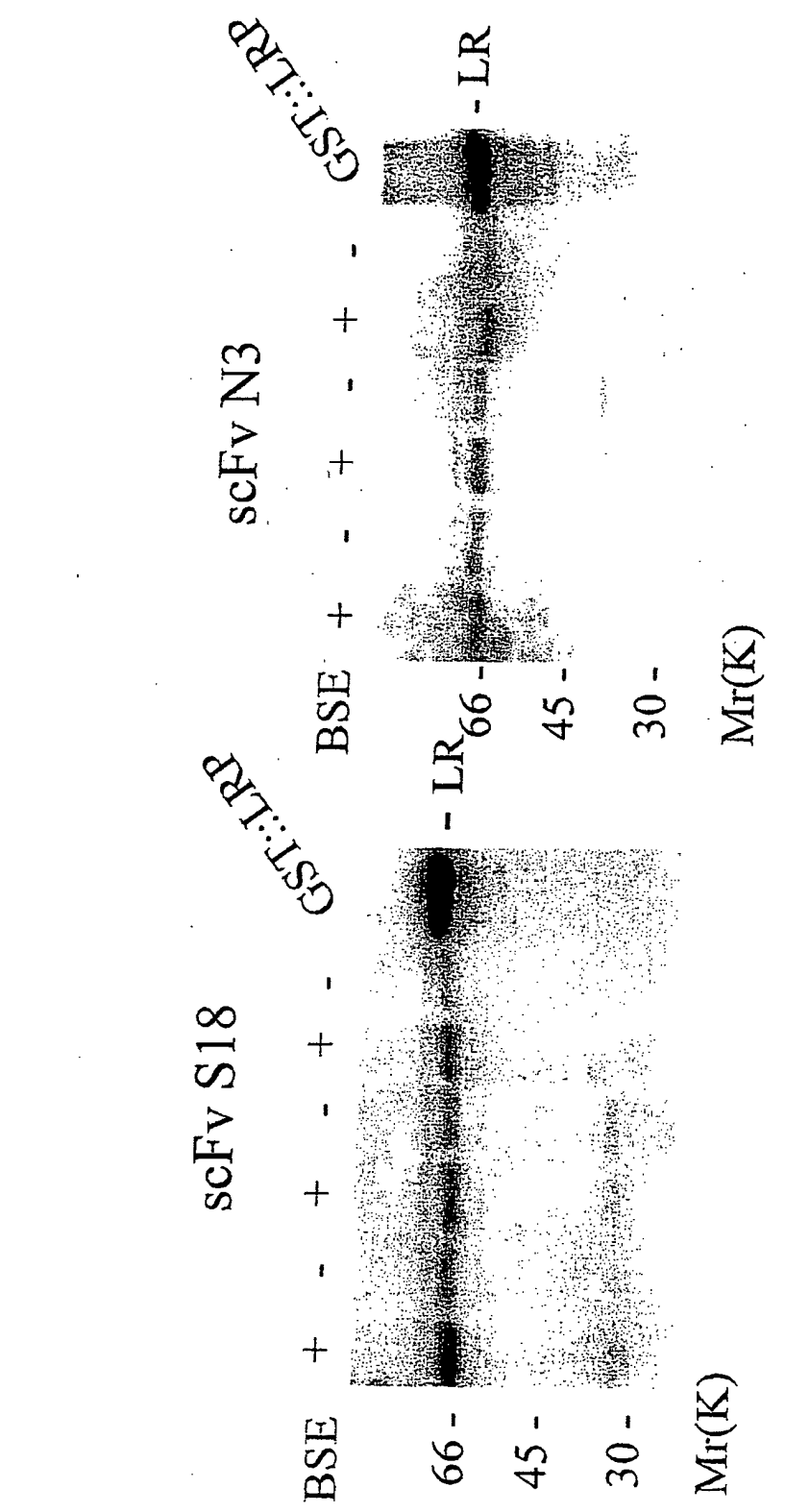

Fig. 15. Recognition of the 67 kDa LR form of the laminin receptor by antibodies S18 and N3 in the cerebraspinal fluid of cattle which are suffering from BSE and healthy cattle. + cattle suffering from BSE; - healthy cattle.

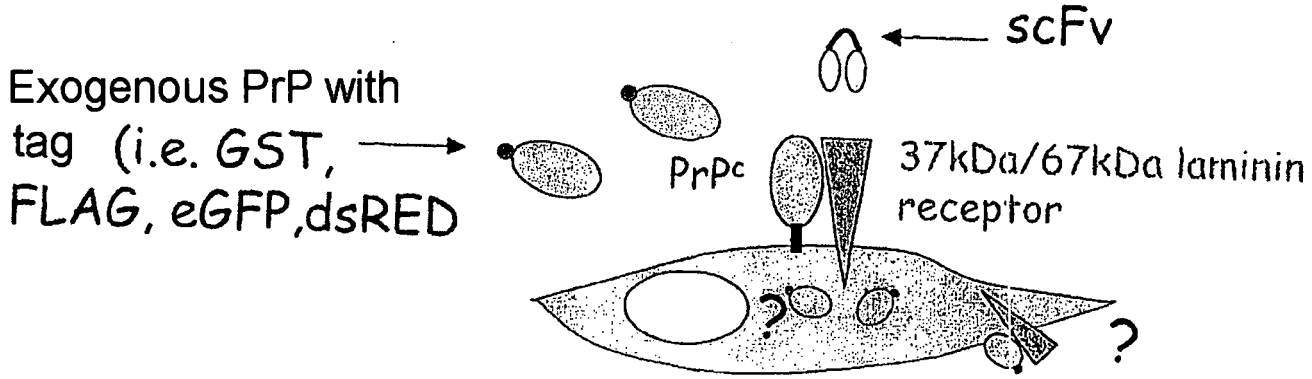

Fig. 16. scFvs S18 and N3 prevent the binding and internalization of exogenously tagged PrP^{C}.

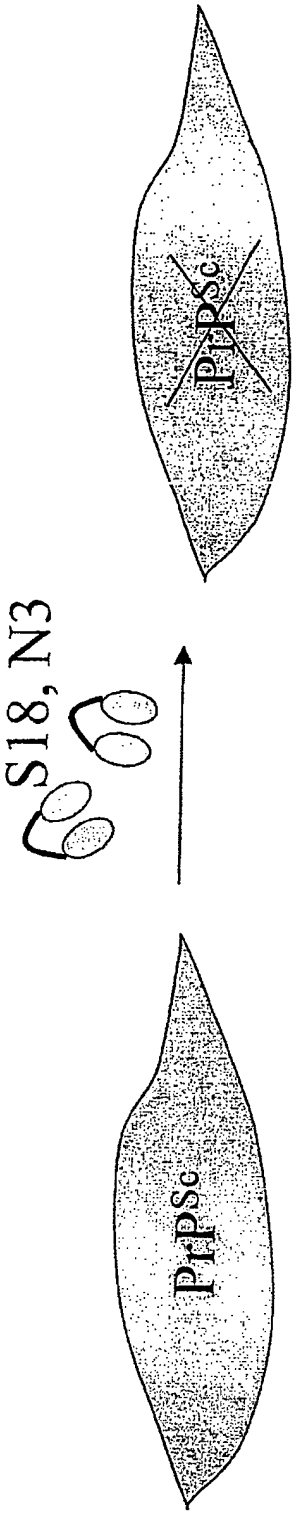

Fig. 17. scFvs S18 and N3 can cure PrP^{Sc}-proliferating cells of PrP^{Sc}.

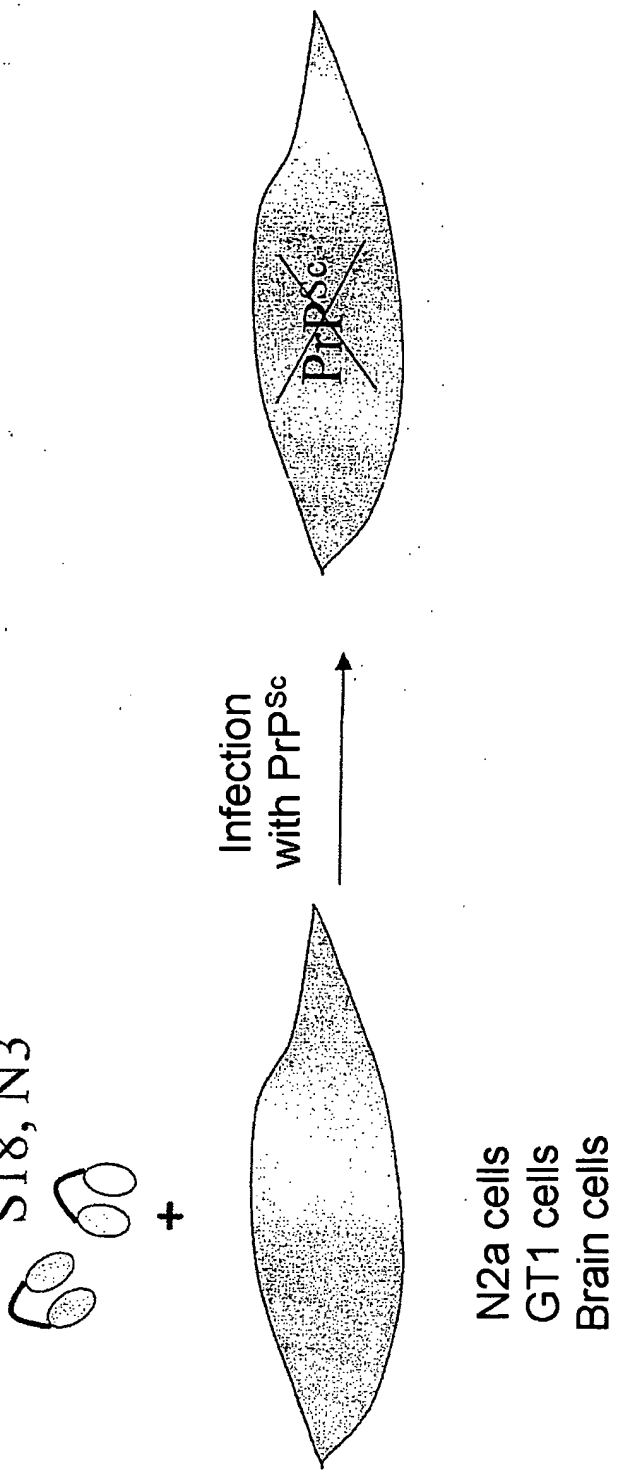

Fig. 18. Preventive effect of scFvs S18 and N3 on scrapie-infectable cells.

A Evaluation of the side effects of scFv (S18/N3) treatment in mice

- Side effects on account of funktional loss of LRP/LR possible

- nonspecific effects possible (i.e. inflammatory response)

B

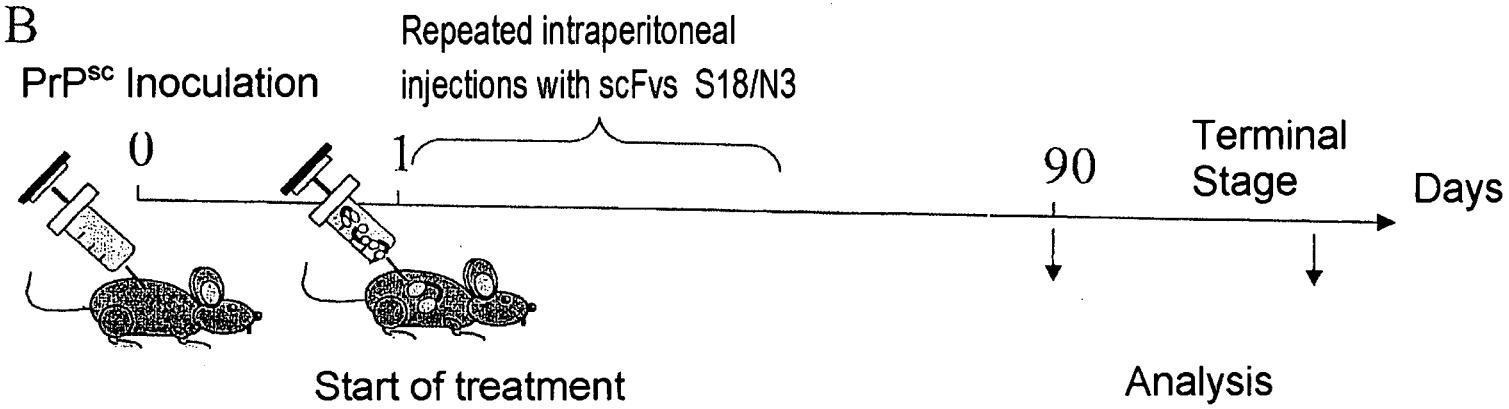

Fig. 19. In vivo effect of the scFv antibodies S18 and N3 in mice after inoculation with PrP^{Sc}. Analysis of the dead time, the PrP^{Sc} accumulation (brain + spleen), performance of psychomotor tests.

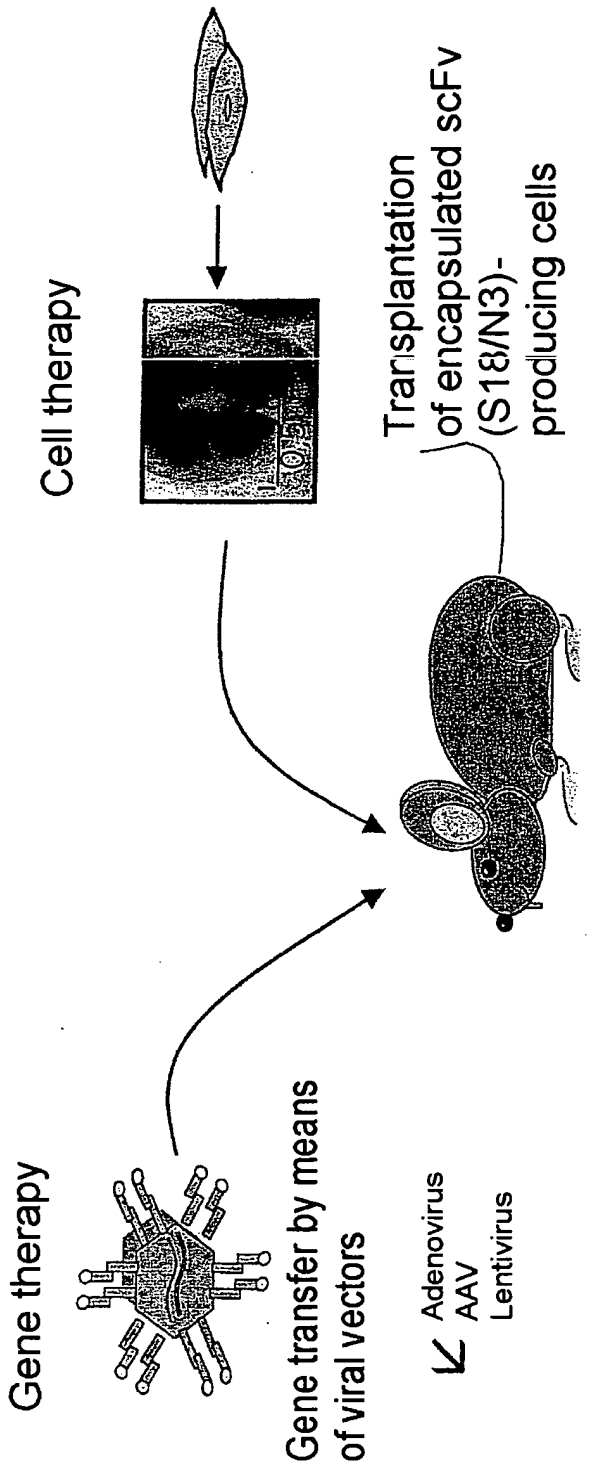

Fig. 20. Gene therapy and cell therapy for the treatment of TSEs in mice.

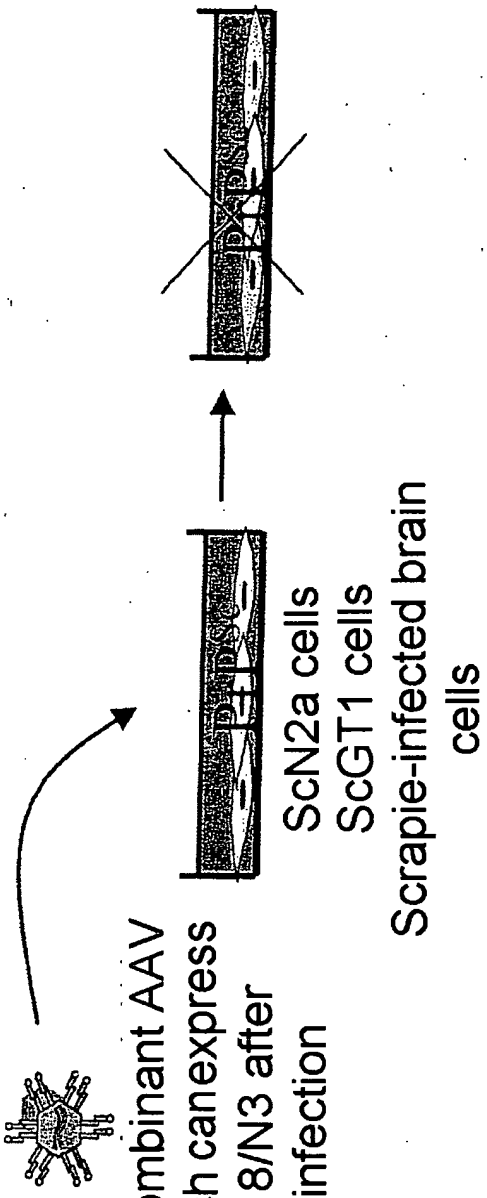

Fig. 21. Gene therapy with the aid of rec. AAVs which express scFvs S18 and N3. Rec. AAV cure scrapie-infected cells of scrapie after infection.

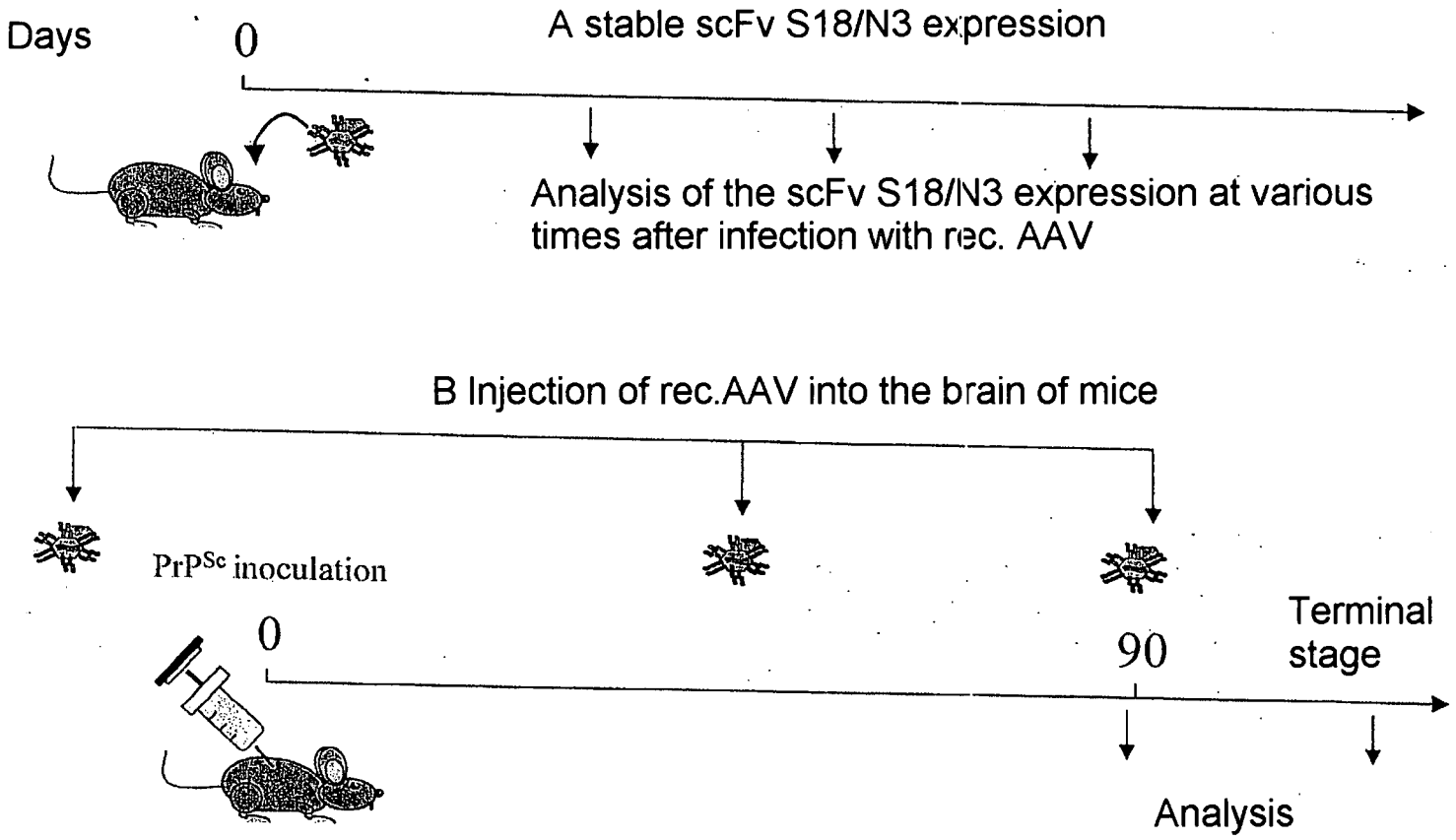

Fig. 22. Gene therapy with the aid of rec. AAVs which express scFvs S18 and N3. (A) Stable expression of scFvs S18 and N3 in the brain of mice. (B) Injection of rec. AAV which express S18/N3 at various times before and after a PrP^{Sc} inoculation.

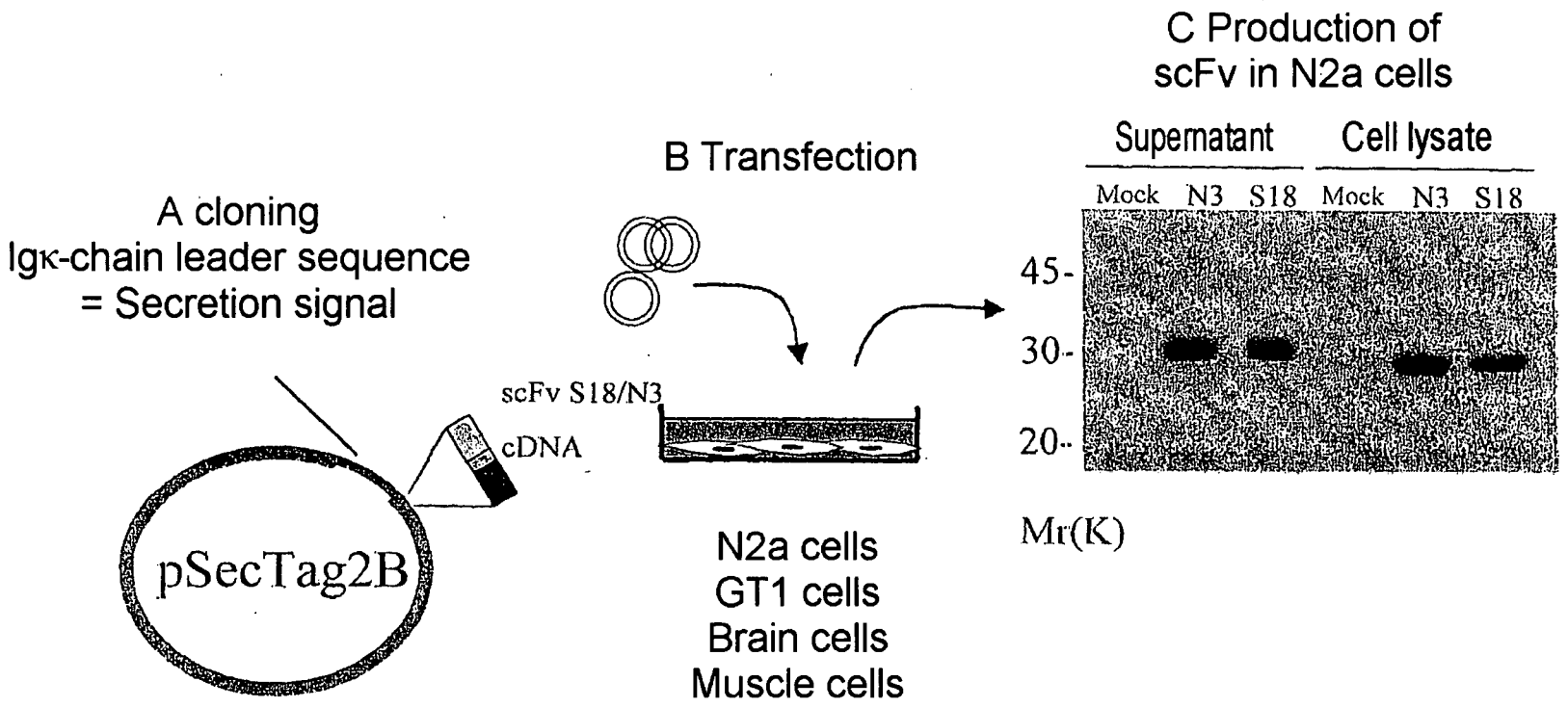

Fig. 23. Cell therapy for the treatment of TSEs in mice. (A) Cloning of scFv S18/N3 cDNA in pSecTag2. (B) Transfection in mammalian cells. (C) Secretion of the scFvs S18 and N3 in the medium of N2a cells.

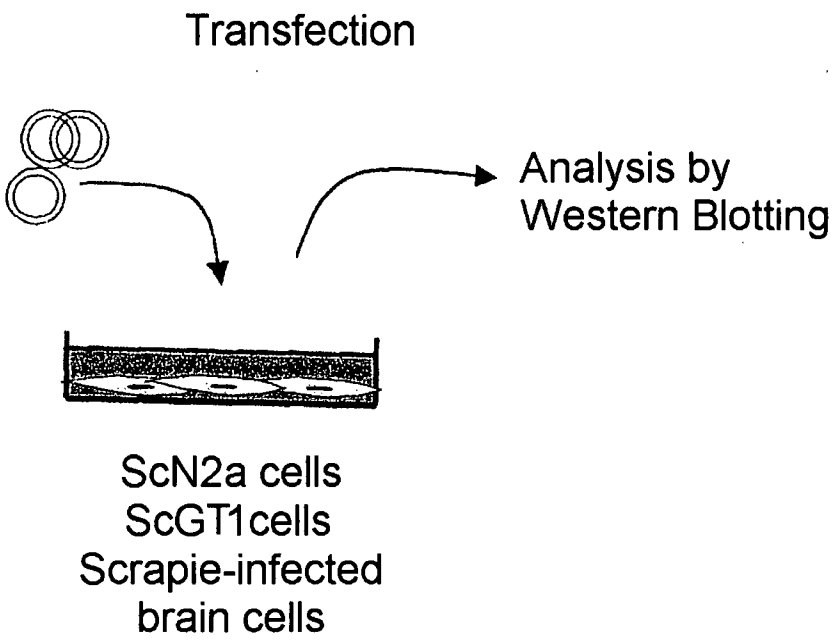

Fig. 24. Cell therapy for the treatment of TSEs in mice. The secretion of scFv S18/N3 from ScN2a/ScGT1cells cures ScN2a/ScGT1 cells of scrapie.

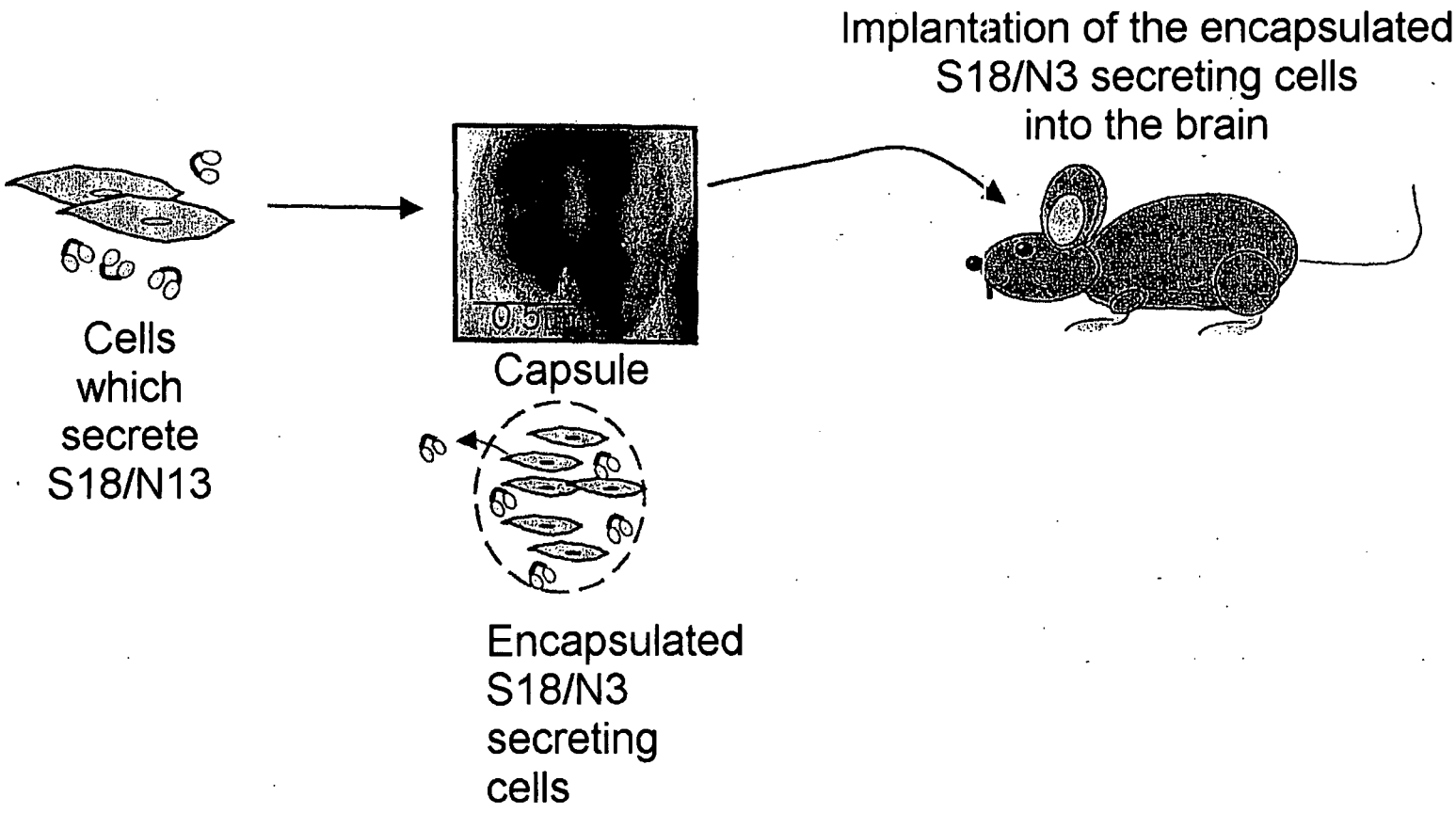

Fig. 25. Cell therapy with the aid of encapsulated cells (i.e. neuronal cells (PC12, N2a, GT1), muscle cells, BHK, NHI3T3, which secrete scFv S18/N3.

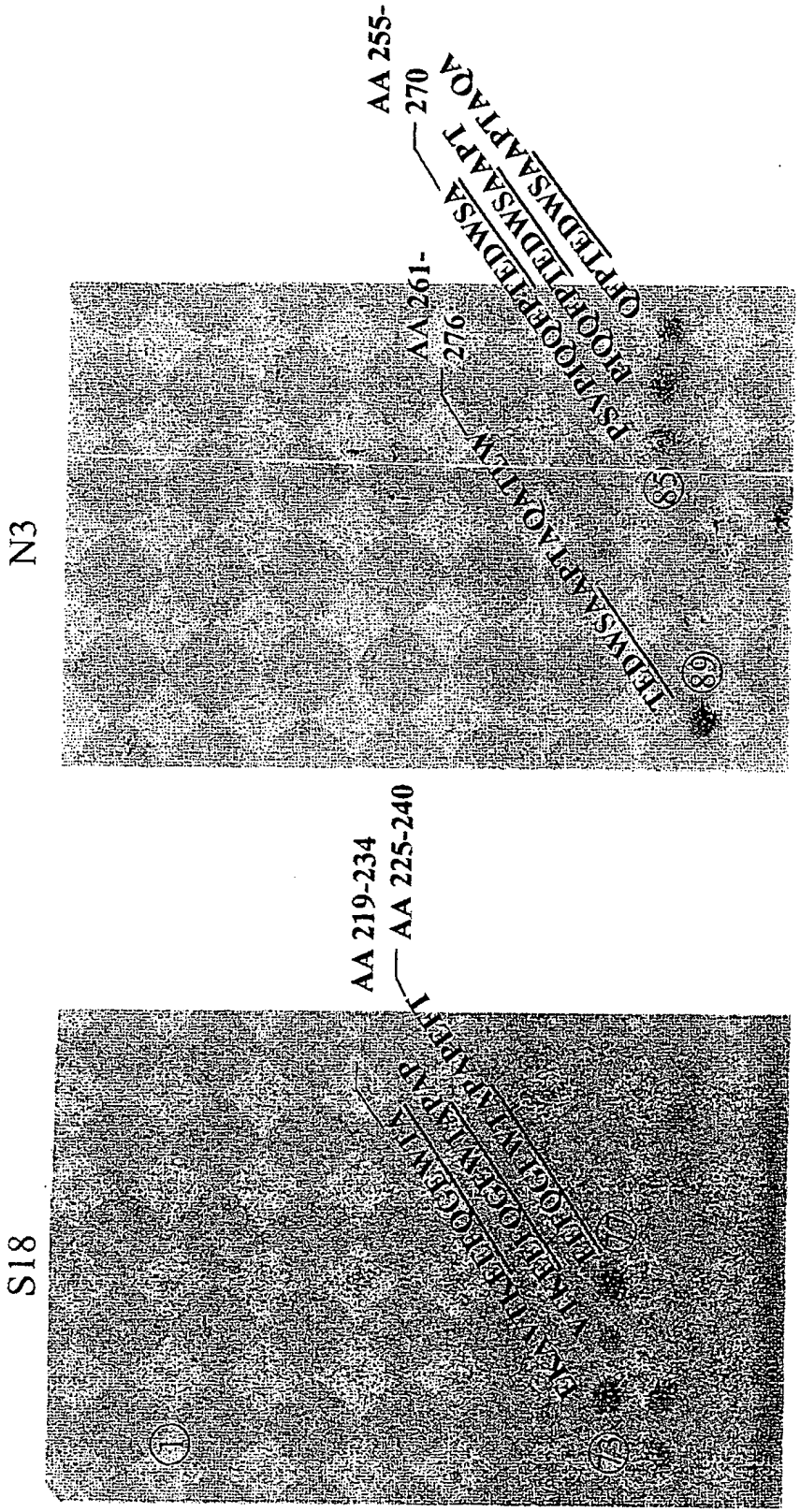

Fig. 26. Epitope mapping of the scFv antibodies S18 and N3.

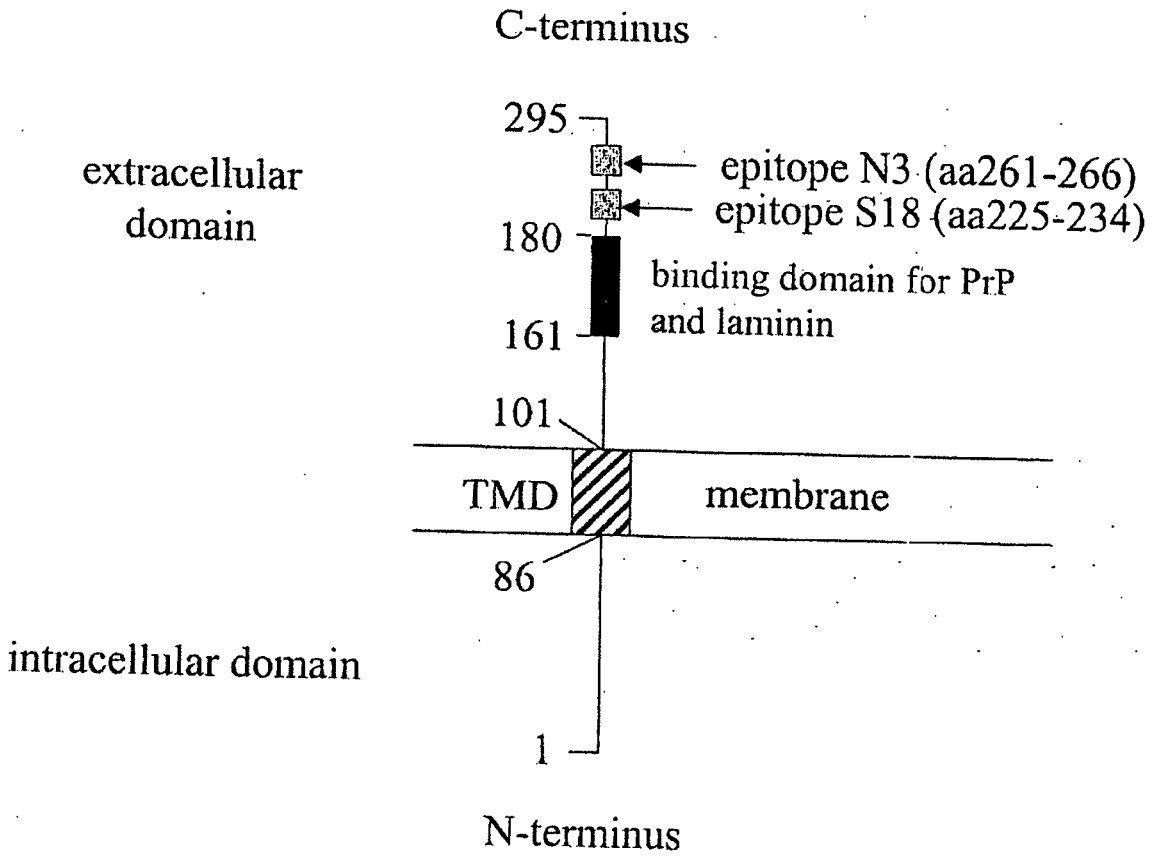

Fig. 27. Schematic representation of the epitope mapping of the scFv antibodies S18 and N3. The epitope aa261-266 is shown, which binds to N3, and the epitope aa225-234), which binds to S18.